DETAILED ACTION

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office Action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission, filed on May 7, 2010, has been entered.

2. Applicant's amendment to the claims, filed on April 13, 2010, has been entered.

Claims 1-53, 75, and 81 have been canceled.

Claim 113 has been canceled.

Claims 54-74, 76-80, and 82-113 are pending.

Claims 54-69, 73, 74, 76, 88-91, 94-105, and 107-111 stand withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on April 6, 2009.

Claims 70-72, 77-80, 82-87, 92, 93, 106, 112, and newly added claim 113 are currently under consideration as they read on the originally elected invention of non-blocking antibodies that bind FcγRIIb of SEQ ID NO:2.

3. This Office Action will be in response to applicant's arguments, filed on April 13, 2010.

The rejections of record can be found in the previous Office Action, mailed on June 23, 2009 and January 13, 2010.

4. Applicant's IDS, filed on July 19, 2010, is considered.

5. In view of applicant's amendment, only following rejections have been set forth herein.

6. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

7. Claim 87 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 87 is indefinite in the recitation of "antibody GB3" and "antibody CE5" because the metes and bounds of the terms describing the antibodies are unclear and ambiguous. The use of "antibody GB3" and "antibody CE5" as the sole means of identifying the claimed antibodies renders the claim indefinite because the terms are merely laboratory designations which do not clearly define the claimed products, since different laboratories may use the same designations to define completely distinct biological materials. Deleting "GB3" and "CE5" would obviate this rejection.

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claims 70-72, 77-80, 82-87, 92, 93, 106, 112, and 113 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an

antibody or antigen-binding fragment thereor, wherein the antibody specifically binds human FcγRIIb in the natural environment of the Fc receptor and does not interfere with immune complex binding to FcγRIIb, and wherein the antibody comprises the following structures:

A) a variable light chain having the amino acid sequence of SEQ ID NO:5,

B) a variable heavy chain having the amino acid sequence of SEQ ID NO:7,

C) a variable light chain having the amino acid sequence of SEQ ID NO:9,

D) a variable heavy chain having the amino acid sequence of SEQ ID NO:11,

E) a variable light chain having the amino acid sequence of SEQ ID NO:5 and a variable heavy chain having the amino acid sequence of SEQ ID NO:7 or SEQ ID NO:11,

F) a variable light chain having the amino acid sequence of SEQ ID NO:9 and a variable heavy chain having the amino acid sequence of SEQ ID NO:7 or SEQ ID NO:11, **OR,**

G) variable light chain CDRs1-3 from the variable light chains of SEQ ID NOs: 7 or 9 and variable heavy chain CDRs 1-3 from the variable heavy chains of SEQ ID NOs: 7 or 11 (must have all six CDRs of which three are from light chain and three from heavy chain).

does not reasonably provide enablement for more. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The claims are drawn to a substance that specifically binds to an artificial peptide or polypeptide comprising a conformationally discriminating epitope (CDE) in its native conformation, wherein the CDE is from SEQ ID NO:2 (representing FcγRIIb), and/or an antibody that specifically binds human FcγRIIb.

The specification discloses that the substance can be any peptides and polypeptides including antibody fragment or derivatives (e.g. see page 21). The specification discloses that FcγRIIb antibodies, e.g. GB3 and CE5 was produced using FcγRIIb-CDE as antigen to immunize mouse (e.g. see Examples 1-2 on pages 25-29). The cDNA encoding the antibody heavy and light chains were determined and corresponding amino acid sequences were disclosed (e.g. see pages 24-25).

The specification does not provide sufficient guidance or directions regarding a a substance that specifically binds a peptide comprising CDE from the SEQ ID NO:2 or an antibody comprises less than all six CDRs and/or in unspecified order. A person skill in the art would not be able to predict which additional CDRs are to be paired together to form a functional antibody with no antigen specificity.

It is well established in the art that the formation of an intact antigen-binding site generally requires the association of the complete heavy and light chain variable regions of a given antibody, each of which consists of three CDRs which provide the majority of the contact residues for the binding of the antibody to its target epitope. The amino acid sequences and conformations of each of the heavy and light chain CDRs are critical in maintaining the antigen binding specificity and affinity which is characteristic of the parent immunoglobulin. It is expected that all of the heavy and light chain CDRs in their proper order and in the context of framework sequences which maintain their required conformation, are required in order to produce a protein having antigen-binding function and that proper association of heavy and light chain variable regions is required in order to form functional antigen binding sites. Even minor changes in the amino acid sequences of the heavy and light variable regions, particularly in the CDRs, may dramatically affect antigen-binding function.

For example Rudikoff et al. (PNAS 1982 Vol 79, pages 1979-1983) teach that the alteration of a single amino acid in the CDR of a phosphocholine-binding myeloma

protein resulted in the loss of antigen-binding function (see entire document, particularly page 1979).

Further, the state of the art at the time the invention was made recognizes even minor changes in the amino acid sequences of the heavy and light variable regions, particularly in the CDRs, may dramatically affect antigen-binding function.

For example, Rader et al. (PNAS. 1998. 95:8910-8915) teach in vitro selection and evolution of antibodies derived from phage display libraries by paring either heavy or light chain of the rodent antibody with human polypeptide library for antibody humanization is unpredictable, and certain antibodies cannot be humanized using this approach; and in addition, antibodies consisting of the same heavy chain paired with light chains that differ in light chain CDR3 and elsewhere in VL can obtain undesired feature of binding different epitopes of the same antigen (see entire document, particularly Discussion on pages 8914-8915). Rader's methods do not result in an antibody solely by keeping CDR3 in the VH defined and randomizing the rest of the VH and VL domain.

Therefore, it is unlikely that the substance and/or antibodies as defined by the claims, which contain not all CDRs in unspecified order would have the required binding function such as "specifically binds to human FcγRIIb in the natural environment of the Fc receptor and does not interfere with immune complex binding to FcγRIIb" or any substances that are not an antibody.

In fact, Koenig et al. (US Patent 7,425,620, reference of record) teach a monoclonal antibody that specifically binds native human FcγRIIb which is endogenously expressed and present on surface of a cell with higher affinity than FcγRIIa (e.g. see column 9-16). Koenig et al. further teach a species of said antibody, 3H7, whose light chain variable region is 92.3% identical in amino acid sequence to the instant SEQ ID NO:5; the instant SEQ ID NO:5 shares at least the same CDR1 sequence to the prior art light chain variable region of 3H7 (see CDR1 location of the instant SEQ ID NO:5 on Figure 5 of the specification as-filed). As such, Koenig et al. also meet the limitations in

claims 83, 84, and 97, encompassing "one or more" CDRs from SEQ ID NO:5 and GB3 according to SEQ ID NOs: 5 and 7 or "a portion thereof having specificity", respectively. Yet, Koenig's full length anti-FcγRIIb antibody blocks the binding of the immune complex binding to FcγRIIb (e.g. see columns 111-113).

As such, the specification provides insufficient direction or guidance regarding how to make and use the claimed substance or antibody as broadly defined by the claims other than ones described above. Undue experimentation would be required to produce the invention commensurate with the scope of the claims from the written disclosure alone.

In view of the quantity of experimentation necessary, the limited working example, the unpredictability of the art, the lack of sufficient guidance in the specification, and the breadth of the claims, it would take undue trials and errors to make

8. Claim 87 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Claim 87 is drawn to antibody GB3 or CE5.

As a required element, the antibodies GB3 and CE5 must be known and readily available to the public or obtainable by a repeatable method set forth in the specification. If they are not so obtainable or available, the enablement requirements of 35 USC 112, first paragraph, may be satisfied by a deposit of the cell lines/hybridomas which produce the GB3 and CE5 antibodies. See 37 CFR 1.1801-1.1809.

In addition to the conditions under the Budapest Treaty, applicant is required to satisfy that all restrictions imposed by the depositor on the availability to the public of the

deposited material will be irrevocably removed upon the granting of a patent in US patent applications.

Amendment of the specification to recite the date of the deposit and the complete name and address of the depository is required. As an additional means for completing the record, applicant may submit a copy of the contract with the depository for deposit and maintenance of each deposit.

If the original deposit is made after the effective filing date of an application for patent, applicant should promptly submit a verified statement from a person in a position to corroborate the fact, and should state, that the biological material which is deposited is a biological material specifically identified in the application as filed, except if the person is an attorney or agent registered to practice before the Office, in which case the statement need not be verified. See MPEP 1.804(b).

It is noted that applicant has provided the protein sequences of the variable light chain and heavy chain of SEQ ID NOs: 5 and 7 for the GB3 antibody and variable light and heavy chain of SEQ ID NOs: 9 and 11 for the CE5 antibody.

However, it is noted that the sequence of an entire immunoglobulin satisfies the biological deposit of said antibodies. Note that satisfaction for the biological deposit of the specific GB3 and CE5 antibodies requires the disclosure and recitation of its entire amino acid sequence and not based upon partial sequences (e.g. variable domains of the antibodies).

9. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted

> on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

10. Claims 70-72, 77-80, 82-87, 92, 93, 106, 112, and newly added 113 are rejected under 35 U.S.C. 102(e) as being anticipated by Koenig et al. (US Patent 7,425,620) as evidenced by the CDRs location of variable light region of mAbGB3 disclosed in Figure 5 of the instant specification and as further evidenced by Veri et al. (Immunology, 2007. 121:392-404) regarding the non-blocking nature of the Fab fragment of 3H7 on right column on page 402.

As stated previously, "*Koenig et al. teach a monoclonal antibody that specifically binds native human FcγRIIb which is endogenously expressed and present on surface of a cell with higher affinity than FcγRIIa (e.g. see column 9-16). Koenig et al. further teach a species of said antibody, 3H7, whose light chain variable region is 92.3% identical in amino acid sequence to the instant SEQ ID NO:5; the instant SEQ ID NO:5 shares at least the same CDR1 sequence to the prior art light chain variable region of 3H7 (see CDR1 location of the instant SEQ ID NO:5 on Figure 5 of the specification as-filed).*

Furthermore, Koenig et al. teach:

A) anti- FcγRIIb antibody that is IgG, IgE, IgM, or IgA (e.g. see column 16),

B) anti- FcγRIIb antibody that is single chain, Fab fragment, F(ab)2 fragment, scFv fragment (e.g. see column 16), bispecific or trispecific antibody (e.g. see column 27),

C) pharmaceutical composition comprising said antibody (e.g. see column 13 and claims 10-13),

D) anti- FcγRIIb antibody that is modified in the Fc region for alteration of glycosylation or amino acid substitutions for enhanced binding affinity towards FcγRs (e.g. see column 32-33),
E) a kit comprising antibody that can be used for diagnosing autoimmune diseases (e.g. see columns 5-6 and 103).

Given that the instant claims (e.g. claim 87) recite a part of the antibody sequence rather than full length of the variable regions, the prior art antibody that is 92.3% identical to the instant SEQ ID NO:5 would read onto the instant claims.

Moreover, given that the prior art antibody has the same structure and antigen specificity as the instant antibody, it would be an inherent property for the prior art antibody to be able to bind a CDE of FcγRIIb."

Applicant's arguments, filed on January 13, 2010, have been fully considered but have not been found persuasive.

Applicant argues that column 10 of Koenig et al shows that the antibodies having higher binding affinity to FcγRIIb than FcγRIIa also block the IgG binding site of the FcγRIIb. As such, applicant argues that the prior art antibodies do not meet the claimed limitation of "does not interfere with the immune complex binding to FcγRIIb" recited in the instant claim 71.

This is not found persuasive for following reasons:

While Koenig et al. teach that the full length 3H7 and 2B6 block immune complex binding to FcγRIIb (e.g. see columns 111-113), Koenig et al. also produced and deposited antibody clones 2D11, 1D5, and 1F2, wherein the antibodies produced by these clones bind FcγRIIb with higher affinity than FcγRIIa (e.g. see column 26).

As evidenced by Veri et al., monomeric Fab 3H7 and other anti-FcγRIIb antibodies including those produced by clones 2D11, 1D5, 1F2 do not interfere with immune complex binding to the FcγRIIB (e.g. see right column on page 395 and right column on page 402).

As such, applicant's arguments have not been found persuasive.

11. No claim is allowed.

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Chun Dahle whose telephone number is 571-272-8142. The examiner can normally be reached on 8:30-5:00. If attempts to reach the examiner by

telephone are unsuccessful, the examiner's supervisors Ram Shukla or Phuong N. Huynh can be reached 571-272-0735 and 571-272-0846, respectively. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Chun Dahle/
Primary Examiner, Art Unit 1644